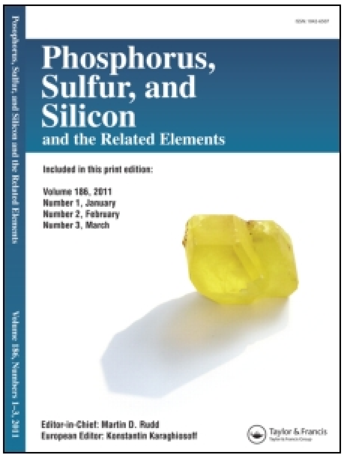

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Novel and Highly Efficient Protection of Aliphatic Alcohols and Phenols with Hexamethyldisilazane in the Presence of $La(NO_3)_3 \cdot 6\ H_2O$

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Novel and Highly Efficient Protection of Aliphatic Alcohols and Phenols with Hexamethyldisilazane in the Presence of $La(NO_3)_3 \cdot 6\ H_2O$

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Aliphatic alcohols and phenols are protected with hexamethyldisilazane in the presence of lanthanum nitrate hexahydrate ($La(NO_3)_3 \cdot 6H_2O$) *in excellent yields at room temperature.*

Keywords Alcohol; hexamethyldisilazane (HMDS); lanthanum nitrate hexahydrate; phenol; trimethylsilyl ether

INTRODUCTION

The role of silyl groups has already been recognized as an important part of organic chemistry from both analytical and synthetic points of view, especially as a protecting group in many syntheses of reasonable complexity.[1] Generally the formation of silyl ethers is achieved by treatment of the corresponding alcohols with silyl chlorides or silyl triflates in the presence of a base,[2] Li_2S,[3] and sometimes a nonionic super base catalyst.[4] However, some of these methods frequently suffer from drawbacks such as the lack of reactivity or the difficulty in removing the ammonium salts derived from the reaction of the by-produced acid and the co-bases during the silylation reaction. 1,1,1,3,3,3-Hexamethyldisilazane (HMDS) is a stable, commercially available, and cheap reagent for trimethylsilylation of hydroxy compounds, giving ammonia as the only byproduct. On the other hand,

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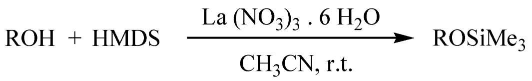
because of easiness in handling and neutrality of this silylating reagent using HMDS does not need special precautions. However, the low silylating power of 1,1,1,3,3,3-hexamethyldisilazane is a main drawback for its application, which needs forceful conditions and long reaction times in many instances. A variety of catalysts such as $(CH_3)_3SiCl$,[5] $ZnCl_2$,[6] complexes of metal chlorides[7] with nitrogen ligands, zirconium sulfophenyl phosphonate,[8] K-10 montmorillonite,[9] and a special type of catalyst with the general formula X^1-NH-X^2, in which at least one of the groups X^1 and X^2 is electron-withdrawing such as an ester or amide group, has also been reported to promote the silylation of a wide range of functional groups using HMDS.[10]

Here we report the use of an efficient and cheap system for the trimethylsilylation of aliphatic alcohols and phenols.

RESULTS AND DISCUSSION

Recently we have reported the trimethylsilylation of alcohols and phenols with HMDS in the presence of $Cu(2,3\text{-tmtppa})^{4+}$ [11], $CuSO_4 \cdot 5\,H_2O$, and anhydrous $FeCl_3$.[12] In continuation of this study we are especially interested in exploring the potential use of a neutral catalyst. Here according to the previous catalytic effect of $La(NO_3)_3 \cdot 6\,H_2O$,[13] we describe a new protocol for the mild and rapid trimethylsilylation of a wide variety of aliphatic alcohols and phenols using HMDS and a catalytic amount of $La(NO_3)_3 \cdot 6\,H_2O$. First, the protection of benzyl alcohol under the catalytic effect of $La(NO_3)_3 \cdot 6\,H_2O$ was studied. Benzyl trimethylsilyl ether was produced immediately in quantitative yield. Employing a 1:1 ratio in acetonitrile at room temperature gave the best results and produced the respective trimethylsilyl ethers in quantitative yields (Table I). We then applied these conditions for the protection of structurally different alcohols and phenols (Scheme 1).

As shown in Table I, this method is very suitable for the conversion of primary, secondary, tertiary, and benzylic alcohols as well as aryl alcohols to the corresponding trimethylsilyl ethers.

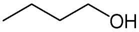
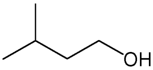
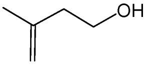
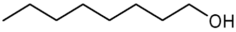
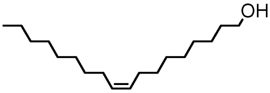
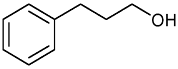
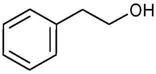
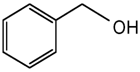
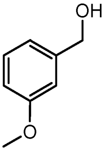
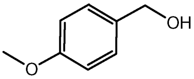
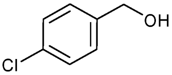
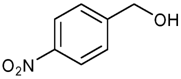
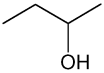
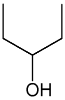
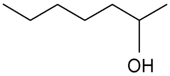
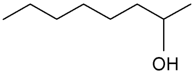
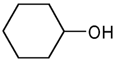


$$\text{ROH} + \text{HMDS} \xrightarrow[\text{CH}_3\text{CN, r.t.}]{\text{La(NO}_3)_3 \cdot 6\,\text{H}_2\text{O}} \text{ROSiMe}_3$$

R: primary, secondary, tertiary alkyl and phenyl

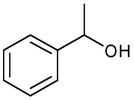
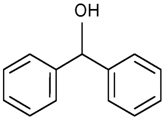
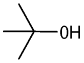
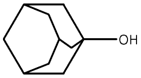
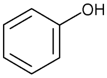
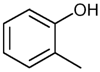
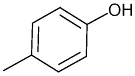
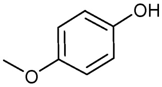
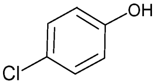
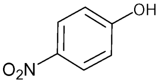
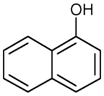
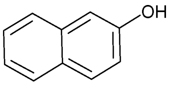
SCHEME 1

TABLE I Trimethylsilylation of Aliphatic Alcohols and Phenols Catalyzed by La $(NO_3)_3 \cdot 6H_2O$ in Dry CH_3CN

Substrate	Conversion%[a]	Isolated yield%
	100	98
	100	97
	100	97
	100	98
	100	95
	100	96
	100	98
	100	98
	100	98
	100	97
	100	98
	100	98
	100	96
	100	95
	100	95
	100	98
	100	97

(Continued on next page)

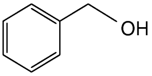
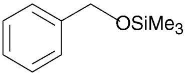
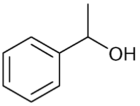
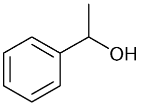
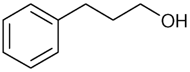
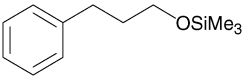
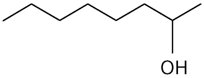
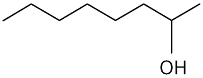
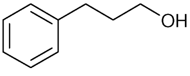
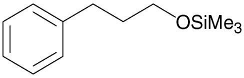
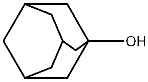
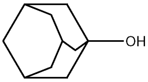
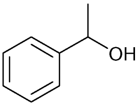
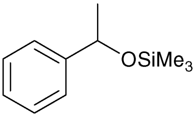
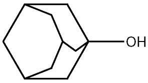
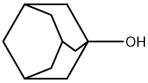
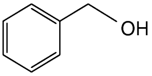
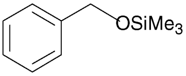
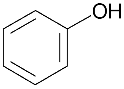
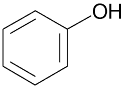
TABLE I Trimethylsilylation of Aliphatic Alcohols and Phenols Catalyzed by La $(NO_3)_3 \cdot 6H_2O$ in Dry CH_3CN *(Continued)*

Substrate	Conversion%[a]	Isolated yield%
	100	97
	85	80
	100	90
	80	73
	90	85
	80	78
	95	90
	90	88
	85	80
	60	58
	70	67
	50	46

[a]GC yield using *n*-octane as internal standard.

To estimate the selectivity of this new method, we studied the reaction of some binary mixtures of substrates. Excellent selectivity was observed in the conversion of primary alcohols to the corresponding trimethylsilyl ethers in the presence of secondary and tertiary alcohols

TABLE II Selective Trimethylsilyl Ether Formation from Different Binary Mixtures

Binary Mixture	Products	Yield (%)^a
		100
		98
		100
		97
		100
		100
		100
		100
		100
		100

^{a}GC yield using *n*-octane as internal standard.

(Table II). Benzyl alcohol is selectively protected with this reagent in the presence of phenol (Table II).

In this article, we have introduced La $(NO_3)_3 \cdot$ 6 H_2O as a novel, efficient, and convenient solid acid catalyst for the trimethylsilylation of hydroxyl groups. The new catalyst is reusable and is easily separated from the reaction mixture. Workup and isolation of the product by this protocol are also straight forward.

EXPERIMENTAL

Chemicals were obtained from Merck and Fluka. FT-IR spectra were recorded with a Perkin Elmer RXI spectrophotometer. ^{1}H NMR spectra were recorded with a Bruker Avance DPX 250 MHz instrument. The products were purified by column chromatography and the purity of the products was determined by GC on a Shimadzu GC 10-A instrument using *n*-octane as internal standard or by thin layer chromatography using silica gel polygram on SIL G/UV 254 plates.

General Procedure for Protection of Alcohols

To a flask containing $La(NO_3)_3 \cdot 6\ H_2O$ (0.004 g, 0.01 mmol) in dry acetonitrile (3–5 mL), HMDS (0.576 g, 1 mmol) was added under stirring at room temperature. Subsequently, the alcohol (1 mmol) was added. GC analysis showed that the reaction was completed immediately. The solvent was evaporated under reduced pressure. Column chromatography of the crude product on silica gel using *n*-hexane as eluent gave the corresponding trimethylsilyl ether in quantitative yield.

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